Cardiovascular Subcommittee of the Pharmacology and Therapeutics Advisory Committee (PTAC)

Meeting held on 27 September 2017

(minutes for web publishing)

Cardiovascular Subcommittee minutes are published in accordance with the *Terms of Reference for the Pharmacology and Therapeutics Advisory Committee (PTAC) and PTAC Subcommittees 2016.*

Note that this document is not necessarily a complete record of the Cardiovascular Subcommittee meeting; only the relevant portions of the minutes relating to Cardiovascular Subcommittee discussions about an Application or PHARMAC staff proposal that contain a recommendation are generally published.

The Cardiovascular Subcommittee may:

(a) recommend that a pharmaceutical be listed by PHARMAC on the Pharmaceutical Schedule and the priority it gives to such a listing;

(b) defer a final recommendation, and give reasons for the deferral (such as the supply of further information) and what is required before further review; or

(c) recommend that PHARMAC decline to list a pharmaceutical on the Pharmaceutical Schedule.

These Subcommittee minutes will be reviewed by PTAC at its meeting on 8 & 9 February 2018, the record of which will be available in due course.

Record of the Cardiovascular Subcommittee of the Pharmacology and Therapeutics Advisory Committee (PTAC) meeting held at PHARMAC on 27 September 2017

Summary of Recommendations

3.2 The Subcommittee noted from PHARMAC staff that candesartan cilexetil is likely to be included in the 2017/18 Tender. The Subcommittee **recommended** PHARMAC remove the Special Authority from candesartan.

3.4 The Subcommittee discussed ranolazine. The Subcommittee considered this a niche drug that would only be used by a few patients with arrhythmia and intractable angina (despite all usual drug and revascularisation treatment options), but it would be a useful drug to have access to. The Subcommittee noted that a form of ranolazine was registered with Medsafe in April 2017 and **recommended** that PHARMAC approach the supplier to seek a funding application.

3.6 The Subcommittee reiterated its previous **recommendation** that rosuvastatin be funded with high priority as a third-line cholesterol lowering agent after treatment failure with, or intolerance to, both simvastatin and atorvastatin. The Subcommittee suggested that failure to reach a target LDL cholesterol of < 2.0 mmol/L at maximal tolerated doses of atorvastatin (80 mg once-daily in most patients) could be a useful criterion to target rosuvastatin to those who would benefit most.

3.8 The Subcommittee **recommended** PTAC review its low priority recommendation for eplerenone considering the high unmet health need of patients requiring a treatment of heart failure who develop gynecomastia on spironolactone, this constituting a distinct group of those with heart failure. Members noted that results of the SNOW trial comparing of eplerenone versus spironolactone in heart failure patients with diabetes were now not expected until 2018. Members considered the results of this study will be useful to evaluate the place of eplerenone in the wider heart failure patient group.

4.3 The Subcommittee noted the significant mortality benefit and good safety profile. The Subcommittee disagreed with PTAC's low priority recommendation and **recommended** that sacubitril with valsartan be funded with a high priority, with a Special Authority as set out by PTAC but with further definition of what "optimal treatments" are including Beta-Blockers, ACE inhibitors, angiotensin receptor blockers and aldosterone antagonists.

4.6 The Subcommittee noted that labetalol tablets are planned for discontinuation by the supplier in mid-2019. Members considered that labetalol is still used and has good safety data in antenatal patients. The Subcommittee noted there is some data for metoprolol and atenolol, but there is not the same experience as with labetalol. The Subcommittee **recommended** PHARMAC seek the advice of the professional bodies for obstetrics and midwifery.

4.9 The Subcommittee noted that ramipril is not currently listed but ramipril is likely to be included in the 2017/18 Tender. Members considered there were no risks around this and it was widely used internationally. Members considered that funding ramipril would assist in the reduction of international divergence in the ACE inhibitor market. The Subcommittee **recommended** that ramipril be listed without restrictions.

5.7 The Subcommittee **recommended** another NOAC was funded for those unable to take dabigatran, especially those with poor renal function, with a high priority.

5.13 The Subcommittee **recommended** that IV aspirin be funded with a high priority.

8.2 The Subcommittee **recommended** that the application for ticagrelor (Brilinta) 60 mg tablets for the prevention of thrombotic events (cardiovascular death, myocardial infarction and stroke) in patients with a history of myocardial infarction and a high risk of developing a thrombotic event be declined.

9.2 The Subcommittee **recommended** that the changes to the ticagrelor or prasugrel Special Authority criteria to allow treatment guided by CYP2C19 genotyping for in patients with acute coronary syndromes (ACS) be deferred until more evidence was available on the clinical outcomes associated with selecting antiplatelet agents based on genetic testing.

10.2 The Subcommittee **recommended** that access to ticagrelor (and prasugrel) be widened to include the prevention of thrombosis post-neurological stenting, with a medium priority.

11.2 The Subcommittee **recommended** that aspirin, atorvastatin, and ramipril combination pills be funded with a medium priority.

12.2 The Subcommittee **recommended** that access to intravenous (IV) nicardipine should be widened to the adult population, with a medium priority.

1 Record of the Previous Cardiovascular Subcommittee Meeting

1.1 The Subcommittee noted and accepted the record of its previous meeting held on 17 February 2016.

1.2 The Subcommittee noted the length of time since its last meeting. The Subcommittee expressed a preference to meet every 12 months, or sooner if there are enough items to discuss.

2 Previous recommendations and action points

Candesartan cilexetil

2.1 The Subcommittee noted from PHARMAC staff that candesartan cilexetil is likely to be included in the 2017/18 Tender. The Subcommittee **recommended** PHARMAC remove the Special Authority from candesartan.

Rosuvastatin

2.2 The Subcommittee discussed rosuvastatin, which both PTAC and the Cardiovascular Subcommittee had given a medium priority in 2009 and 2010 respectively. Rosuvastatin is currently prioritised by PHARMAC. Members noted that rosuvastatin was commonly used overseas and there was a risk of international divergence possibly causing supply risks. Members noted anecdotal evidence of lower myalgia risk with rosuvastatin. Members considered that while there are currently three funded statins and ezetimibe available, more options would be preferable and that rosuvastatin would be a preferred agent when compared to ezetimibe especially in statin-resistant disease such as familial hypercholesterolaemia. Members discussed the value of pravastatin; some considered it of little value, while others considered it had niche applications when P450 interactions were a concern. Members considered it may be preferable to obtain more targeted funding of rosuvastatin to limit budget impact.

2.3 The Subcommittee reiterated its previous **recommendation** that rosuvastatin be funded with high priority as a third-line cholesterol lowering agent after treatment failure with, or intolerance to, both simvastatin and atorvastatin. The Subcommittee suggested that failure to reach a target LDL cholesterol of < 2.0 mmol/L at maximal tolerated doses of atorvastatin could be a useful criterion to target rosuvastatin to those who would benefit most.

Eplerenone

2.4 The Subcommittee noted their previous high priority recommendation for funding of eplerenone for those with heart failure with an EF<40% who have severe disabling mastalgia. The Subcommittee noted that PTAC had considered eplerenone following a further submission from the supplier and gave it a low priority recommendation for funding for all patients 'intolerant to spironolactone', not just gynecomastia. The Subcommittee noted from PHARMAC staff that eplerenone is likely to be included in the 2017/18 Tender.

2.5 The Subcommittee **recommended** PTAC review its low priority recommendation for eplerenone considering the high unmet health need of patients requiring a treatment of heart failure who develop gynecomastia on spironolactone, this constituting a distinct group of those with heart failure. Members noted that results of the SNOW trial comparing of eplerenone versus spironolactone in heart failure patients with diabetes were now not expected until 2018. Members considered the results of this study will be useful to evaluate the place of eplerenone in the wider heart failure patient group.

3 Therapeutic Group Review

3.1 The Subcommittee noted a review of funded pharmaceuticals relevant to cardiology provided by PHARMAC staff.

Review of PTAC recommendations

Sacubitril with valsartan

3.2 The Subcommittee noted PTAC's discussion of sacubitril with valsartan. Members considered that the PARADIGM-HF trial (N Engl J Med. 2014;371:993-1004) was a well-conducted trial using an appropriate comparator for the New Zealand setting (enalapril 10 mg twice daily). The Subcommittee noted this dose of enalapril was consistent with international and NZ practice and has proven efficacy in large trials, allowing indirect comparisons with other trials in heart failure.

3.3 The Subcommittee noted the significant mortality benefit and good safety profile. The Subcommittee disagreed with PTAC's low priority recommendation and **recommended** that sacubitril with valsartan be funded with a high priority, with a Special Authority as set out by PTAC but with further definition of what "optimal treatments" are including Beta-Blockers, ACE inhibitors, angiotensin receptor blockers and aldosterone antagonists.

3.4 The Subcommittee considered that it would be appropriate to restrict initiation to specialists only as all patients should have an echocardiogram prior to commencement. Members noted that access to echocardiograms is constrained in some areas and this has the potential for inequities.

4 Matters Arising and correspondence

NOACs

4.1 The Subcommittee noted the paper on novel oral anticoagulants (NOACs, also called direct oral anticoagulants or DOACs) from PHARMAC staff and correspondence from clinicians supporting the availability of an additional NOAC to meet a need for a dabigatran alternative.

4.2 The Subcommittee considered that there is an unmet clinical need in the patient group of those who are not able to take dabigatran because of intolerance or contraindications, noting that this would likely be about 15% of treated patients.

4.3 The Subcommittee considered it would be worthwhile seeking a funding application for edoxaban.

4.4 The Subcommittee considered that clinicians are unlikely to prescribe NOACs based on the availability of reversal agents. Members noted that andexanet alfa is difficult to administer and may have a limited effect.

4.5 The Subcommittee noted that there was significant international divergence in New Zealand's NOAC use and considered that it would be appropriate to fund at least two NOACs.

4.6 Members discussed possible restriction criteria for a second NOAC as a second-line alternative to the currently listed dabigatran. Various options were raised, including whether a warfarin trial with inability to maintain 50% time in therapeutic range was appropriate, although members had reservations with this option due to

the difficulties of managing warfarin in some patients. The Subcommittee considered the following criteria would be appropriate:

1. Patient has persistent moderate renal impairment (CrCl <50 ml/min) in the absence of a reversible cause; or
2. Documented evidence of severe and persistent gastrointestinal intolerance requiring discontinuation of dabigatran after an adequate trial period.

4.7 The Subcommittee **recommended** another NOAC was funded for those unable to take dabigatran, especially those with poor renal function, with a high priority.

IV aspirin

4.8 The Subcommittee noted that PHARMAC had received a clinician funding application for intravenous aspirin (lysine acetyl salicylate) for use during interventional neuro-radiology procedures to reduce risk of thromboembolism when intracranial stent or coils are being used.

4.9 The Subcommittee noted that intravenous aspirin would also be useful for acute interventional cardiology procedures when the patient is unable to take oral aspirin or it is unreasonable to delay the procedure for oral absorption.

4.10 Members considered that there was a lack of reasonable alternatives in the acute interventional procedure setting. The most likely alternative in patients unable to take oral aspirin is to await insertion of a nasogastric tube and a delay the intervention for 20 to 30 minutes awaiting the absorption of oral aspirin and clopidogrel. Members noted rectal aspirin may be used when oral aspirin could not be administered, but there is still an absorption delay and there was uncertainty about product was availability.

4.11 The Subcommittee considered that about 150 patients each year would use IV aspirin if it was permitted for interventional cardiology procedures, plus about another 50 patients per year for interventional neuro-radiology procedures

4.12 The Subcommittee noted there may be a risk of wider use by acute stroke services and this should be reviewed by the Neurological Subcommittee. A funding application would be required if wider access is sought beyond the acute interventional procedure setting.

4.13 The Subcommittee **recommended** that IV aspirin be funded with a high priority.

5 Treatment of pulmonary arterial hypertension (PAH)

5.1 The Subcommittee reviewed a paper from PHARMAC on proposed changes to the PAH treatment algorithm.

5.2 The Subcommittee considered that PAH is a progressive disease for which patients would likely be on treatment permanently or until transplant. The Subcommittee noted that about 90% of people start treatment on sildenafil.

Members considered that funded treatment options lagged significantly behind those available in other countries.

5.3 The Subcommittee noted that PTAC had recommended that patients need only try one monotherapy, instead of two, before progressing to dual therapy. Members considered that the PAH Panel was in practice taking this approach currently.

5.4 The Subcommittee noted the proposal that all patients with NYHA/WHO Functional Class II PAH severity be eligible, and supported this change to allow starting treatment earlier.

5.5 The Subcommittee noted the PTAC recommendation to fund IV epoprostenol for highly severe PAH in Section B of the Pharmaceutical Schedule. The Subcommittee considered that epoprostenol has several potential adverse effects but in general is well tolerated and provides survival benefits. Members considered that IV epoprostenol would be preferred over iloprost despite requiring insertion of a central line. Members noted epoprostenol's more consistent delivery of therapy and the practical difficulties with iloprost which requires 6-8 nebulisations a day which led to practical difficulties for daily activities. It was considered that if funded epoprostenol would replace most or all of iloprost use.

5.6 The Subcommittee noted the PTAC recommendation to fund triple therapy for patients on the lung transplant list, and discussed triple therapy generally. The Subcommittee considered that, while it recognised triple therapy combined treatments with different mechanisms of action, evidence for triple therapy was limited and the Subcommittee did not consider triple therapy should be funded except in the lung transplant list setting.

5.7 The Subcommittee discussed other restrictions on access, and noted that a number of tests were currently required to verify progression and the severity of a patient's PAH. The Subcommittee considered it may be more appropriate to rely on the expert opinion of the treating clinicians rather than requiring a submission to the Panel, Members of the Subcommittee who were also on the PAH Panel considered that it was not necessary for the Panel to review applications for the now lower-cost sildenafil. However, members also considered that expert oversight by the Panel prior to initiation of therapy provided useful data and that it ensured that these treatments are funded only for patients with PAH, rather than patients with elevated pulmonary artery pressures due to left heart or underlying lung disease, where there is no evidence of benefit.

6 Ticagrelor 60 mg

Application

6.1 The Subcommittee reviewed a supplier funding application from AstraZeneca for ticagrelor (Brilinta) 60 mg tablets for the prevention of thrombotic events (cardiovascular death, myocardial infarction and stroke) in patients with a history of myocardial infarction and a high risk of developing a thrombotic event.

Recommendation

6.2 The Subcommittee **recommended** that the application for ticagrelor (Brilinta) 60 mg tablets for the prevention of thrombotic events (cardiovascular death, myocardial infarction and stroke) in patients with a history of myocardial infarction and a high risk of developing a thrombotic event be declined.

Discussion

6.3 The Subcommittee noted that PTAC had considered extended ticagrelor treatment beyond 12 months following an acute coronary syndrome (ACS) event with 90 mg twice daily by removal of the Special Authority. The Subcommittee noted that PTAC had referred this or the ticagrelor 60 mg application to the Cardiovascular Subcommittee for further consideration.

6.4 The Subcommittee noted Ticagrelor 90 mg tablets have been listed on the Pharmaceutical Schedule since 2013 for 12 months treatment following an ST-elevation or a non-ST-elevation acute coronary syndrome. The supplier now seeks a listing for ticagrelor 60 mg tablets on the Pharmaceutical Schedule for use following that 12 months' treatment in high risk patients, that is, commencing 1-3 years after the myocardial infarction.

6.5 The Subcommittee noted that about 18,000 New Zealanders each year had a ACS event, with roughly half requiring percutaneous coronary intervention (PCI). The Subcommittee noted myocardial infarction incidence is declining.

6.6 The Subcommittee noted that there was one high-quality RCT in support of the proposal, the PEGASUS-TIMI 54 study (Bonaca et al. NEJM 2015; 19:1791-1800), however it provided only weak evidence of benefit for extended treatment with ticagrelor over placebo. The Subcommittee considered this trial demonstrated a very small benefit for ticagrelor in terms of reduced cardiovascular death over placebo for the 3-year study period (7.77% versus 9.04%), and this benefit was offset with an increase in the risk of bleeding (2.3% versus 1.05%).

6.7 The Subcommittee noted the large trial of twelve or 30 months of dual anti-platelet therapy (DAPT) after drug-eluting stent placement following myocardial Infarction (Mauri et al. N Engl J Med. 2014;371:2155-66). This trial involved 9961 randomised patients, who mostly received either everolimus-eluting or paclitaxel-eluting stents, who after 12 months either continued DAPT or moved to aspirin alone. The Subcommittee noted the long-term results were favourable in terms of stent thrombosis and major adverse cardiovascular and cerebrovascular events, but this translated into little or no reduction in cardiovascular death and there was an increased risk of bleeding.

6.8 The Subcommittee considered that DAPT extended beyond 12 months after ACS is not yet shown to be superior to aspirin alone. The Subcommittee noted that there was a view that extended DAPT beyond 12 months could be beneficial in those with a high-thrombotic risk and a low bleeding risk, but considered that clopidogrel was currently funded without restriction, so this was possible, despite this approach lacking strong evidence of overall benefit. The Subcommittee noted that extended DAPT beyond 12 months was likely overused currently.

6.9 The Subcommittee considered that there is insufficient evidence to conclude that extended DAPT beyond 12 months with ticagrelor is superior to using clopidogrel, and when combined with the lack of strong supporting evidence for extended DAPT beyond 12 months, the Subcommittee did not support funding its funding at this time.

7 Ticagrelor or prasugrel treatment based on CYP2C19 genotyping

Application

7.1 The Subcommittee reviewed a funding application from a clinician for CYP2C19 genotyping in patients with acute coronary syndromes (ACS) to guide antiplatelet management.

Recommendation

7.2 The Subcommittee **recommended** that the changes to the ticagrelor or prasugrel Special Authority criteria to allow treatment guided by CYP2C19 genotyping for in patients with acute coronary syndromes (ACS) be deferred until more evidence was available on the clinical outcomes associated with selecting antiplatelet agents based on genetic testing.

Discussion

7.3 The Subcommittee noted PHARMAC had received a clinician funding application for CYP2C19 genotyping in patients with acute coronary syndromes (ACS) to guide antiplatelet management.

7.4 The Subcommittee noted one of the applicants is the owner of the testing instrumentation and patented technologies required for the proposed CYP2C19 genotyping and that the testing is currently only available at Waitemata DHB.

7.5 The Subcommittee noted that PHARMAC staff had communicated with the applicant that the funding of the genotype testing is likely to be considered outside of PHARMACs remit, although PHARMAC could consider consider possible changes to the Special Authority criteria currently in place for ticagrelor and/or prasugrel.

7.6 The Subcommittee noted that current Special Authority restrictions for ticagrelor allow 12 months of funded treatment post ST-elevation or a non-ST-elevation acute coronary syndrome for all patients. The Subcommittee noted that the applicant has suggested cost savings may be made by restricting access by allowing ticagrelor access only in ‘clopidogrel non-responders’.

7.7 The Subcommittee noted that current Special Authority restrictions for prasugrel, are that a patient needs to either be clopidogrel-allergic or have experienced cardiac stent thrombosis whilst on clopidogrel. The Subcommittee noted that the applicant has requested wider access for ‘clopidogrel non-responders’ following PCI.

7.8 The Subcommittee noted that there was a theoretical basis for guiding antiplatelet therapy by determining poor responders to clopidogrel (using various approaches, including CYP2C19 genotyping), and that there was some limited evidence of worse outcomes in this group. The Subcommittee however considered that there remained insufficient evidence for additional population health benefits by personalising antiplatelet therapy, as this was yet to be stablished in a significant clinical trial. Members noted that a large-scale trial confirming this personalised treatment approach was unlikely to occur.

7.9 The Subcommittee noted that there was no evidence to suggest that the differences observed for ticagrelor versus clopidogrel in patients with ACS in the pivotal PLATO trial was due to generic polymorphisms.

8 Ticagrelor or prasugrel post-neurological stenting

Application

8.1 The Subcommittee reviewed a funding application from a clinician for ticagrelor (and prasugrel) as a funded option for the prevention of thrombosis post-neurological stenting.

Recommendation

8.2 The Subcommittee **recommended** that access to ticagrelor (and prasugrel) be widened to include the prevention of thrombosis post-neurological stenting, with a medium priority.

Discussion

8.3 The Subcommittee noted PHARMAC had received a clinician funding application for the prevention of thrombosis post-neurological stenting in individuals who have demonstrated clopidogrel resistance using the P2Y12 (VerifyNow) assay.

8.4 The Subcommittee noted that PHARMAC has received six applications under NPPA for use of ticagrelor (two) and prasugrel (four) since October 2015 for use post-neurological stenting in individuals who have demonstrated clopidogrel resistance using the P2Y12 (VerifyNow) assay.

8.5 The Subcommittee noted the clinical and financial consequences of thromboembolism/occlusion in this setting are very significant, with more effective prevention likely to result in reduced hospitalisation.

8.6 The Subcommittee noted that 6 to 12 months of antiplatelet treatment is required in about 200 people per year if all patients receiving neurological stents are commenced on ticagrelor. Of those patients, 15-20% are likely to be non-responders to clopidogrel, for which one of the ways this can be detected is using the VerifyNow assay.

8.7 The Subcommittee noted that there was a theoretical basis for using an alternative antiplatelet in this very high need setting. Some Members expressed their concern

about the lack of evidence, but noted that a clinical trial of good quality was unlikely to occur due to the small number of patients.

8.8 The Subcommittee concluded that given the small numbers and very high-risks associated with thrombus formation, it was reasonable to support funding based largely on expert opinion, despite the low quality and weak evidence of benefit provided in the published papers provided with the application (Gandhi et al. J Neurointerv Surg. 2014;6:567-77; Oran et al. J Neurointerv Surg. 2015;7:357-62; Hanel et al. J Neurointerv Surg. 2014;6(4):320-2).

9 Aspirin, atorvastatin and ramipril combination pill (Trinomia polypill)

Application

9.1 The Subcommittee reviewed an application from Te Arai BioFarma for funding of aspirin, atorvastatin, and ramipril combination pills (Trinomia).

Recommendation

9.2 The Subcommittee **recommended** that aspirin, atorvastatin, and ramipril combination pills be funded with a medium priority.

Discussion

9.3 The Subcommittee considered that the health need of patients in this population was severe and important despite the availability of all components, or another in the class, separately. The Subcommittee noted a study showing that patients who do not adhere to statins have higher event rates such as stroke death. Members considered that need was particularly high in Māori and Pacific peoples, who have higher rates of non-adherence to medications alongside higher disease burden from cardiovascular disease.

9.4 The Subcommittee reviewed the Cochrane review (Bahiru et al, Cochrane Database of Systematic Reviews 2017, Issue 3. Art. No.: CD009868). The Subcommittee considered that the Cochrane review showed that polypills improved adherence, but did not demonstrate improvements in clinical benefits. Members also noted that the review showed more adverse events with polypills. The Subcommittee noted that none of the polypills looked at in the Cochrane review were the same combination of medicines as in Trinomia.

9.5 The Subcommittee considered that the strength and quality of evidence in the adherence trials was of good quality, however they may have been limited by the fact they were performed in a primary prevention population so may have had worse compliance than those taking for secondary prevention.

9.6 The Subcommittee noted that some patients would still need to take multiple pills even if Trinomia were funded, as they take more than three treatments. Members discussed if this would limit the improvements to adherence. Members also noted the risks and harms with polypharmacy in the elderly, including difficulties

differentiating which parts of multiple-component treatments were likeliest to be causing which apparent adverse effects and that combination treatments made deprescribing more difficult.

9.7 The Subcommittee noted that the doses of atorvastatin and aspirin were fixed, but that ramipril could be titrated. Members considered that the dose of atorvastatin was too low for use as secondary prevention, but had no issues with the dose of aspirin. The Subcommittee considered that funding Trinomia might assist with moving patients' use of ACE inhibitors away from cilazapril.

9.8 The Subcommittee compared the increase in cost for the combination product to other funded combination products and considered the increased cost was greater than for asthma combination products. The Subcommittee noted that funding Trinomia would however reduce costs to the patient, or their family/whānau, as it reduces dispensing fees.

9.9 The Subcommittee considered that funding Trinomia would improve adherence in patients otherwise taking the same medications separately, and that despite trial data this improvement in adherence might lead to an improvement in clinical outcomes. It was based on this improvement that the Subcommittee based its recommendation for this specific combination.

9.10 The Subcommittee discussed the appropriate listing restrictions. The Subcommittee considered that the restrictions proposed by the applicant were not practical. Members considered that without restrictions, uptake would be high, and difficult to estimate. The Subcommittee considered that treatment should be guided by cardiovascular risk-assessment rather than any set clinical criteria and thus open-listing would be preferred. The Subcommittee considered that 50% of the patients currently taking all three classes would likely change to a combination product if available.

10 Intravenous nicardipine

Application

10.1 The Subcommittee reviewed a clinician application seeking to widen access to intravenous (IV) nicardipine for perioperative use as antihypertensive/vasodilator in adults.

Recommendation

10.2 The Subcommittee **recommended** that access to intravenous (IV) nicardipine should be widened to the adult population, with a **medium** priority.

Discussion

10.3 The Subcommittee noted that IV nicardipine is currently listed in the HML with restrictions, limiting its use to only the paediatric population. The Subcommittee considered that previous advice given to PHARMAC to limit the use of IV

nicardipine to children may have been due to the availability of multiple suitable alternatives for adults.

10.4 The Subcommittee noted that nicardipine belongs to the dihydropyridine class of calcium channel blockers, and that its use in hospitals would be to induce a rapid decrease in the patient's blood pressure. The Subcommittee noted that there are a number of funded alternatives currently listed in the HML which could be used in a similar setting, such as IV nitroprusside, IV labetalol, IV nimodipine and IV glycerol trinitrate (GTN). The Subcommittee noted that IV nimodipine belongs to the same drug class and is likely to have similar mechanisms of action as nicardipine (both are dihydropyridine calcium channel blockers).

10.5 The Subcommittee noted that IV nicardipine is fast acting with more rapid onset than nitroprusside and easier to prepare and administer. It was noted that a 15-minute improvement in patient response time was clinically significant. The Subcommittee noted that while IV nitrates also had a fast onset of action, they were associated with more side effects. Labetalol was noted to be contraindicated in asthmatics. The Subcommittee considered that IV nicardipine was an established medicine, and that its use would be in a monitored setting, and that there would be little additional risk if its use were widened to the adult population.

10.6 The Subcommittee noted that Maori and Pacific people were likely to have higher rates of acute hypertension, but that data had not been presented to support this.

10.7 The Subcommittee noted the applicants estimate that 500 patients per annum might benefit from IV nicardipine. The Subcommittee considered this estimate may be an over estimate due to the availability of suitable alternatives and clinician preferences.

10.8 The Subcommittee did not consider that the proposal would create any significant changes in health-sector expenditure beyond the cost of the drug.

10.9 The Subcommittee noted that a comparison of costs and benefits with IV nimodipine may be appropriate.